54. (Amended) A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 55, and complements of SEQ ID NO: 55; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

REMARKS

Applicants submit this response to the Office Action dated April 18, 2001, Paper No. 17. Favorable reconsideration of the subject patent application is respectfully requested in view of the above amendments and the following remarks. Following the amendments, claims 33, 44 and 54-88 are pending in the application with claims 53-55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85 and 87 being in independent format.

Claims 55-88, drawn to subject matter previously recited in claims 33, 44, 53 and 54, have been added to the application. Claims 33, 44, 53 and 54 have been amended to recite subject matter now recited in claims 55-88. Claim 54 has also been amended to correct a typographical error in the previously filed Amendment and Reply. It is urged that support for all the above amendments may be found throughout the specification as originally filed and that none of the amendments constitute new matter. Applicants submit that the above amendments are not made for reasons of patentability, but rather to focus prosecution on certain aspects of the invention.

Claims 33 and 44 stand rejected under 35 USC §112, first paragraph, as lacking an adequate description. Specifically, the Examiner states that claims 33 and 44 "are directed to encompass gene sequences, full length genes and open reading frames"... (Office Action, page 3, lines 10-11. This rejection is respectfully traversed.

The Examiner supports the ground of rejection by stating that the species that are specifically disclosed are not representative of the genus, because the genus allegedly is highly

variant. (Office Action, page 3, lines 14-15.) According to the Examiner, the specification only discloses SEQ ID NO: 55, 56, 59-65 and 67. Claims 33 and 34 both relate to SEQ ID NO: 55.

Claim 33 depends from claim 53. Claim 53 recites that at least one of the oligonucleotide primers is specific for SEQ ID NO: 55 or a complement thereof. Without acquiescing to the ground of rejection applicants have amended claim 33 to recite "between about 10 and 40" contiguous nucleotides of SEQ ID NO: 55. Applicants submit that this language is fully supported by the application as filed, at, for example, page 27, lines 29-31, which states, "[o]ligonucleotide primers and/or probes which may be usefully employed in the inventive diagnostic methods preferably have at least about 10-40 nucleotides."

Claim 44 depends from claim 54. Claim 54 recites that the oligonucleotide probe is specific for SEQ ID NO: 55 or a complement thereof. Without acquiescing to the ground of rejection, applicants have amended claim 44 to recite "between about 10 and 40" contiguous nucleotides of SEQ ID NO: 55. The amendment to claim 44 is supported in the specification, for example at page 27, lines 29-31.

It is urged that one of skill in the art, on being provided with the instant specification, would readily appreciate that the applicants were indeed in possession of the presently claimed invention at the time the application was filed, and that the rejection of claims 33 and 44 under 35 USC §112, first paragraph, may thus be properly withdrawn.

Claim 53 stands rejected under 35 USC §103(a) as being unpatentable over US Patent 5,536,648 to Kemp in view of US Patent 5,709,999 to Shattuck-Eidens. This rejection is respectfully traversed.

Kemp teaches the use of oligonucleotide primers in polymerase chain reactions (PCR) to detect the present of a target DNA in a biological sample, such as blood and body tissues. Kemp does not teach or suggest the use of oligonucleotide primers specific for the presently recited SEQ ID NO: 55, 56, 59-65 and 67 in the detection of breast cancer. Shattuck-Eidens discloses a breast cancer susceptibility gene that has 60.5% local similarity to SEQ ID NO: 62. The Examiner asserts that this gene would hybridize to SEQ ID NO: 62.

Applicants note that, following the above amendments, methods for the detection of breast cancer using oligonucleotide primers specific for SEQ ID NO: 62 are recited in newly added claim 63. Claim 63 clearly recites a method comprising contacting a biological sample

with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is **specific** for either SEQ ID NO: 62 or a complement of SEQ ID NO: 62. It is submitted that a sequence having only 60.5% local similarity to SEQ ID NO: 62 does not constitute a primer that is specific for SEQ ID NO: 62. Furthermore, applicants note that while the Examiner asserts that the sequence of Shattuck-Eidens would hybridize to SEQ ID NO: 62, the Examiner has not provided any evidence demonstrating that a gene having only 60.5% local similarity to a given sequence would in fact hybridize to that sequence.

It is respectfully submitted that neither the teachings of Kemp nor of Shattuck-Eidens, taken either singly or in combination, would render the presently claimed methods obvious to one of skill in the art, and that the rejection of claim 53 under 35 USC §103(a) may thus be properly withdrawn.

Claims 33, 44, 53 and 54 stand rejected under 35 USC §103(a) as being unpatentable over US Patent 5,536,648 to Kemp in view of Billing-Medel (Gencore Accession no. V31990, from WO 98/18945). This rejection is respectfully traversed.

Following the above amendments, claims to the detection of breast cancer by contacting a biological sample with an oligonucleotide probe specific for SEQ ID NO: 56 are no longer pending in the application.

The teachings of Kemp are discussed above. The Examiner asserts that Billing-Medel teaches a nucleic acid sequence associated with breast cancer that has 99.7% local similarity to SEQ ID NO: 56, and that contains at least about 15 contiguous nucleotides of SEQ ID NO: 56. Following the above amendments, the pending claims are drawn, in part, to methods for the detection of breast cancer comprising contacting a biological sample with at least two oligonucleotide primers specific for SEQ ID NO: 56 in a polymerase chain reaction. It is submitted that Billing-Medel do not teach or suggest two primers that would specifically amplify the sequence of SEQ ID NO: 56 as recited in the presently pending claims.

Applicants submit that the teachings of Kemp and Billing-Medel would not render the presently claimed methods obvious to one of skill in the art and that this rejection of the claims under 35 USC §103(a) may thus be properly withdrawn.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "**Version with markings to show changes made**".

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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Version with markings to show changes made

In the Claims:

The following new claims have been added:

--55. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein the oligonucleotide primers are specific for a sequence selected from the group consisting of: SEQ ID NO: 56 and complements of SEQ ID NO: 56; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

56. The method of claim 55, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 56.

57. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a sequence selected from the group consisting of: SEQ ID NO: 59 and complements of SEQ ID NO: 59; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

58. The method of claim 57, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 59.

59. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a sequence selected from the group consisting of: SEQ ID NO: 60 and complements of SEQ ID NO: 60; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

60. The method of claim 59, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 60.

61. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a sequence selected from the group consisting of: SEQ ID NO: 61 and complements of SEQ ID NO: 61; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

62. The method of claim 61, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 61.

63. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a sequence selected from the group consisting of: SEQ ID NO: 62 and complements of SEQ ID NO: 62; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

64. The method of claim 63, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 62.

65. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a sequence selected from the group consisting of: SEQ ID NO: 63 and complements of SEQ ID NO: 63; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

66. The method of claim 65, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 63.

67. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a sequence selected from the group consisting of: SEQ ID NO: 64 and complements of SEQ ID NO: 64; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

68. The method of claim 67, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 64.

69. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a sequence selected from the group consisting of: SEQ ID NO: 65 and complements of SEQ ID NO: 65; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

70. The method of claim 69, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 65.

71. A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a sequence selected from the group consisting of: SEQ ID NO: 67 and complements of SEQ ID NO: 67; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

72. The method of claim 71, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of SEQ ID NO: 67.

73. A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 59 and complements of SEQ ID NO: 59; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

74. The method of claim 73 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of SEQ ID NO: 59.

75. A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 60 and complements of SEQ ID NO: 60; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

76. The method of claim 75 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of SEQ ID NO: 60.

77. A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 61 and complements of SEQ ID NO: 61; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

78. The method of claim 77 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of SEQ ID NO: 61.

79. A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 62 and complements of SEQ ID NO: 62; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

80. The method of claim 79 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of SEQ ID NO: 62.

81. A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 63 and complements of SEQ ID NO: 63; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

82. The method of claim 81 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of SEQ ID NO: 63.

83. A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 64 and complements of SEQ ID NO: 64; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

84. The method of claim 83 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of SEQ ID NO: 64.

85. A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 65 and complements of SEQ ID NO: 65; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

86. The method of claim 87 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of SEQ ID NO: 65.

87. A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: SEQ ID NO: 67 and complements of SEQ ID NO: 67; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.

88. The method of claim 89 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of SEQ ID NO: 67.--

Claims 33, 44, 53 and 54 have been amended as follows:

33. (Three times amended) The method of claim 53, wherein at least one of the oligonucleotide primers comprises [at least] <u>between</u> about 10 <u>and 40</u> contiguous nucleotides of [a sequence selected from] SEQ ID NO[S]: 55[, 56, 59-65 and 67].

44. (Three times amended) The method of claim 54 wherein the oligonucleotide probe comprises [at least] <u>between</u> about [15]<u>10 and 40</u> contiguous nucleotides of [a sequence selected from the group consisting of] SEQ ID NO[S]: 55[, 56, 59-65 and 67].

53. (Amended) A method for detecting breast cancer in a patient comprising:

(a) contacting a biological sample from a patient with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotides is specific for a sequence selected from the group consisting of: [nucleotide sequences recited in] SEQ ID NO: 55[, 56, 59-65 and 67;] and complements of [said nucleotide sequences] SEQ ID NO: 55; and

(b) detecting in the sample a polynucleotide sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting breast cancer.

54. (Amended) A method for detecting breast cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide probe specific for a sequence selected from the group consisting of: [nucleotide sequences recited in] SEQ ID NO[S]: 55[56, 59-65 and 67], and complements of [said nucleotide sequences and sequences that hybridize to a sequence of] SEQ ID NO: 55[, 56, 59-65 and 67 under moderately stringent conditions]; and

(c) detecting in the sample a polynucleotide sequence that hybridizes to the oligonucleotide probe, thereby detecting breast cancer in the patient.